

## PATENT COOPERATION TREATY

OB 1727509  
18C 11/4/97

PCT

NOTIFICATION CONCERNING  
AMENDMENTS OF THE CLAIMS(PCT Rule 62 and  
Administrative Instructions, Section 417)

## From the INTERNATIONAL BUREAU

To:

United States Patent and Trademark  
Office  
(Box PCT)  
Crystal Plaza 2  
Washington, DC 20231  
ETATS-UNIS D'AMERIQUE

In its capacity as International Preliminary Examining Authority

Date of mailing: 27 May 1997 (27.05.97)	
International application No.: PCT/US96/14250	International filing date: 28 August 1996 (28.08.96)
Applicant: NEW YORK MEDICAL COLLEGE et al	

The International Bureau hereby informs the International Preliminary Examining Authority that no amendments under Article 19 have been received by the International Bureau (Administrative Instructions, Section 417)

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NOV 20 1997  
G.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorised officer:  Martine Lee Telephone No.: (41-22) 730.91.11
Facsimile No.: (41-22) 740.14.35	Form PCT/I/B/337 (July 1992)

001525489

08/20/97

**Copy for the receiving Office (RO/US)**

9500

PCT/US96/14250

## PATENT COOPERATION TREATY

PGT

**NOTIFICATION OF THE RECORDING  
OF A CHANGE**

(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

Date of mailing (day/month/year) 12 June 1997 (12.06.97)		ETATS-UNIS D'AMERIQUE	
Applicant's or agent's file reference 1075PCT		<b>IMPORTANT NOTIFICATION</b>	
International application No. PCT/US96/14250		International filing date (day/month/year) 28 August 1996 (28.08.96)	
<p><b>1.</b> The following indications appeared on record concerning:</p> <p><input checked="" type="checkbox"/> the applicant    <input type="checkbox"/> the inventor    <input type="checkbox"/> the agent    <input type="checkbox"/> the common representative</p>			
Name and Address <b>NEW YORK MEDICAL COLLEGE</b> Valhalla, NY 10595 United States of America		State of Nationality <b>US</b>	
		State of Residence <b>US</b>	
		Telephone No.	
		Facsimile No.	
<p><b>2.</b> The International Bureau hereby notifies the applicant that the following change has been recorded concerning:</p> <p><input type="checkbox"/> the person    <input type="checkbox"/> the name    <input checked="" type="checkbox"/> the address    <input type="checkbox"/> the nationality    <input type="checkbox"/> the residence</p>			
Name and Address <b>NEW YORK MEDICAL COLLEGE</b> Office of Research Administration Administration Building Room 202 Grasslands Avenue Valhalla, NY 10595 United States of America		State of Nationality	
		State of Residence	
		Telephone No.	
		Facsimile No.	
<p><b>3.</b> Further observations, if necessary:</p>   			
<p><b>4.</b> A copy of this notification has been sent to:</p> <p><input checked="" type="checkbox"/> the receiving Office                      <input type="checkbox"/> the designated Offices concerned</p> <p><input type="checkbox"/> the International Searching Authority              <input checked="" type="checkbox"/> the elected Offices concerned</p> <p><input checked="" type="checkbox"/> the International Preliminary Examining Authority              <input type="checkbox"/> other:</p>			

<p><b>The International Bureau of WIPO</b>  <b>34, chemin des Colombettes</b>  <b>1211 Geneva 20, Switzerland</b></p> <p>Facsimile No.: (41-22) 740.14.35</p>	<p><b>Authorized officer</b></p> <p><b>Martine Lee</b></p>
	<p>Telephone No.: (41-22) 338.83.38</p>

## PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

Date of mailing (day/month/year) 12 June 1997 (12.06.97)
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## From the INTERNATIONAL BUREAU

To:

MacWRIGHT, Robert, S.  
Skadden, Arps, Slate, Meagher &  
Flom  
919 Third Avenue  
New York, NY 10022  
ETATS-UNIS D'AMERIQUE

Applicant's or agent's file reference 1075PCT	<b>IMPORTANT NOTIFICATION</b>
International application No. PCT/US96/14250	International filing date (day/month/year) 28 August 1996 (28.08.96)

## 1. The following indications appeared on record concerning:

the applicant     the inventor     the agent     the common representative

Name and Address NEW YORK MEDICAL COLLEGE Valhalla, NY 10595 United States of America	State of Nationality US	State of Residence US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

## 2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

the person     the name     the address     the nationality     the residence

Name and Address NEW YORK MEDICAL COLLEGE Office of Research Administration Administration Building Room 202 Grasslands Avenue Valhalla, NY 10595 United States of America	State of Nationality	State of Residence
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

## 3. Further observations, if necessary:

## 4. A copy of this notification has been sent to:

<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned
<input checked="" type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer  Martine Lee
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

United States Patent and Trademark  
Office  
(Box PCT)  
Crystal Plaza 2  
Washington, DC 20231  
ETATS-UNIS D'AMERIQUE

in its capacity as selected Office

**RECEIVED**

NOV 19 1997

Date of mailing (day/month/year) 27 May 1997 (27.05.97)	Applicant's or agent's file reference 1075PCT
International application No. PCT/US96/14250	Priority date (day/month/year) 30 August 1995 (30.08.95)
International filing date (day/month/year) 28 August 1996 (28.08.96)	<b>GROUP 1800</b>
Applicant DARZYNKIEWICZ, Zbigniew et al	

1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:

26 March 1997 (26.03.97)

in a notice effecting later election filed with the International Bureau on:

\_\_\_\_\_

2. The election  was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer  Martine Lee  Telephone No.: (41-22) 730.91.11
Faxsimile No.: (41-22) 740.14.35	1525487
Form PCT/IB/331 (July 1992)	

# PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To: ROBERT S. MACWRIGHT  
 SKADEN, ARPS, SLATE  
 MEAGHER & FLOM  
 919 THIRD AVENUE  
 NEW YORK, NY 10022

**PCT**

## NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

Date of Mailing (day/month/year)	<b>18 DEC 1996</b>
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Applicant's or agent's file reference  1075PCT	FOR FURTHER ACTION See paragraphs 1 and 4 below
International application No.  PCT/US96/14250	International filing date (day/month/year)  28 AUGUST 1996
Applicant  NEW YORK MEDICAL COLLEGE	

1.  The applicant is hereby notified that the international search report has been established and is transmitted herewith.
- Filing of amendments and statement under Article 19:**  
 The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):
- When?** The time limit for filing such amendments is normally 2 months from the date of transmittal of the international search report; however, for more details, see the notes on the accompanying sheet.
- Where?** Directly to the International Bureau of WIPO  
 34, chemin des Colombettes  
 1211 Geneva 20, Switzerland  
 Facsimile No.: (41-22) 740.14.35
- For more detailed instructions, see the notes on the accompanying sheet.
2.  The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.
3.  With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:
- the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
  - no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.
4. Further action(s): The applicant is reminded of the following:

Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in rules 90 bis 1 and 90 bis 3, respectively, before the completion of the technical preparation for international publication.

Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the ISA/US  Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Address of International Bureau  DIANNE REES
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196

## PATENT COOPERATION TREATY

**PCT**

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 1075PCT	<b>FOR FURTHER ACTION</b>	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No. PCT/US96/14250	International filing date (day/month/year) 28 AUGUST 1996	(Earliest) Priority Date (day/month/year) 30 AUGUST 1995
Applicant NEW YORK MEDICAL COLLEGE		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 4 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1.  Certain claims were found unsearchable (See Box I).
2.  Unity of invention is lacking (See Box II).
3.  The international application contains disclosure of a nucleotide and/or amino acid sequence listing and the international search was carried out on the basis of the sequence listing
  - filed with the international application.
  - furnished by the applicant separately from the international application.
    - but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.
    - transcribed by this Authority.
4. With regard to the title,  the text is approved as submitted by the applicant.
  - the text has been established by this Authority to read as follows:
5. With regard to the abstract,
  - the text is approved as submitted by the applicant.
  - the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.
6. The figure of the drawings to be published with the abstract is:
 

Figure No. \_\_\_\_\_

  - as suggested by the applicant.
  - because the applicant failed to suggest a figure.
  - because this figure better characterizes the invention.

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US96/14250

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :C12Q 1/68, 1/70; C12P 19/34; C07H 21/04; C07K 16/00  
US CL :435/6, 5, 91.1, 91.2; 536/24.3; 530/388.21

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/6, 5, 91.1, 91.2; 536/24.3; 530/388.21

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Extra Sheet.

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JIRIKOWSKI, G.F. In situ hybridization of semithin Epon sections with BrdU labelled oligonucleotide probes. Histochemistry. June 1990. Volume 94, Number 1, pages 187-190, especially page 188, column 2.	1-4 ---- 5-20
X	JIRIKOWSKI, G.F. et al. Immunocytochemistry of 5-bromo-2' deoxyuridine labelled oligonucleotide probes: A novel technique for in situ hybridization. Histochemistry. Volume 91, Number 1, pages 51-53, especially page 51, column 2.	1-4 ---- 5-20
Y	US, 5,053,336 A (VANDERLAAN et al) 01 October 1991, see entire document.	1-20
Y	US, 4,851,331 A (VARY et al) 25 July 1989, column 10.	5-11

 Further documents are listed in the continuation of Box C.

See patent family annex.

- \* Special categories of cited documents:
- \*A\* document defining the general state of the art which is not considered to be of particular relevance
  - \*E\* earlier document published on or after the international filing date
  - \*L\* document which may throw doubt on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
  - \*O\* document referring to an oral disclosure, use, exhibition or other means
  - \*P\* document published prior to the international filing date but later than the priority date claimed
- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- \*&\* document member of the same patent family

Date of the actual completion of the international search

09 DECEMBER 1996

Date of mailing of the international search report

18 DEC 1996

Name and mailing address of the ISA/US  
Commissioner of Patents and Trademarks  
Box PCT

W. L. Gentry, D.C., U.S.A.

Facsimile No. (703) 305-5230

Authorized officer

DIANNE REES

Telephone No. (703) 308-0196

Form PCT/ISA/210 (second sheet)(July 1992)\*

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US96/14250

## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US, 4,780,406 A (DOLBEARE et al) 25 October 1988, see entire document.	12-20
Y,P	US, 5,500,432 A (NICOLAOU et al) 19 March 1996, see Figure 1.	12-20

INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US96/14250

B. FIELDS SEARCHED

Electronic data bases consulted (Name of data base and where practicable terms used):

APS, BIOSIS, BIOTECHABS, BIOBUSINESS, CANCERLIT, CABA, CAPLUS, DRUGU, EMBASE, MEDLINE,  
TOXLINE, TOXLIT, SCISEARCH, USPATFULL, WPIDS, JAPIO, IFIPAT  
search terms: halogenated deoxyribonucleotides, brominated deoxyribonucleotides, BrdU, BrdUTP, BrdUMP,  
halogenated nucleosides, apoptosis, flow cytometry, end-labeling, end-labelling, TdT, or terminal deoxynucleotidyl  
transferase.

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US96/14250

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :C12Q 1/68, 1/70; C12P 19/34; C07H 21/04; C07K 16/00  
US CL :435/6, 5, 91.1, 91.2; 536/24.3; 530/388.21

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/6, 5, 91.1, 91.2; 536/24.3; 530/388.21

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
Please See Extra Sheet.

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JIRIKOWSKI, G.F. In situ hybridization of semithin Epon sections with BrdU labelled oligonucleotide probes. Histochemistry. June 1990. Volume 94, Number 1, pages 187-190, especially page 188, column 2.	1-4 ---- 5-20
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Y	US, 4,851,331 A (VARY et al) 25 July 1989, column 10.	5-11

 Further documents are listed in the continuation of Box C. See patent family annex.

Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance		
"E" earlier document published on or after the international filing date	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&"	document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

09 DECEMBER 1996

Date of mailing of the international search report

18 DEC 1996

Name and mailing address of the ISA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231  
Facsimile No. (703) 305-3230Authorized officer  
DIANNE REES  
Telephone No. (703) 308-0196

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US96/14250

## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US, 4,780,406 A (DOLBEARE et al) 25 October 1988, see entire document.	12-20
Y,P	US, 5,500,432 A (NICOLAOU et al) 19 March 1996, see Figure 1.	12-20

**INTERNATIONAL SEARCH REPORT**

International application No. PCT/US96/14250
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**B. FIELDS SEARCHED**

Electronic data bases consulted (Name of data base and where practicable terms used):

APS, BIOSIS, BIOTECHABS, BIOBUSINESS, CANCERLIT, CABA, CAPLUS, DRUGU, EMBASE, MEDLINE,  
TOXLINE, TOXLIT, SCISEARCH, USPATFULL, WPIDS, JAPIO, IFIPAT  
search terms: halogenated deoxyribonucleotides, brominated deoxyribonucleotides, BrdU, BrdUTP, BrdUMP,  
halogenated nucleosides, apoptosis, flow cytometry, end-labeling, end-labelling, TdT, or terminal deoxynucleotidyl  
transferase.